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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/445,328	12/07/1999	KUBER T. SAMPATH	CIBT-P01-514	9813

28120 7590 12/16/2002

ROPES & GRAY
ONE INTERNATIONAL PLACE
BOSTON, MA 02110-2624

EXAMINER

ROMEO, DAVID S

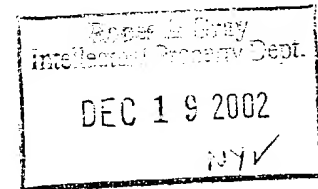
ART UNIT PAPER NUMBER

1647

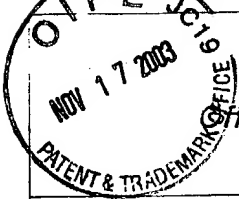
DATE MAILED: 12/16/2002

14

Please find below and/or attached an Office communication concerning this application or proceeding.



R&G
R&G
Docket No. CIBT-P01-514
Resp. to non-final OA
Stat. Deadline: due 3/16/03 & exp 6/16/03



Office Action Summary

Application No.

09/448,323

Applicant(s)

SAMPATH ET AL.

Examiner

David S Romeo

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 August 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-52 is/are pending in the application.
- 4a) Of the above claim(s) 1,3,4,21,22,25,26,28-34 and 39-52 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2,5-20,23,24,27 and 35-38 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 1-52 are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|----------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: |

DETAILED ACTION

Claims 1-52 are pending.

Applicant's election with traverse of Group X, the species OP-1, the species the mature
5 form of OP-1, the species pre-renal causes of acute renal failure, the species decreased cardiac
output, and the species intravenous administration in Paper No. 12 is acknowledged. The
traversal is on the ground(s) that will be allowed to prosecute a generic linking claim, claim 2 is
a generic linking claim, claim 2 is generic to an OP/BMP renal therapeutic agent, group I is not
independent of groups II-XLV, group I and groups II-XLV do not define patentably distinct
10 inventions, the OP/BMP agents have structural similarity, the examination of groups I-XLV
would not impose an undue search burden, group X relates to groups I-IX, groups XIX-XXVII
and groups XXVIII-XXXVI would be ways to treat subjects in acute renal failure or delay
dialysis. This is not found persuasive because restriction was required under 35 U.S.C. 121 and
372 and group X lacks a technical feature that defines a contribution which each of the claimed
15 inventions, considered as a whole, makes over the prior art, as indicated by the prior art
rejections below, and therefore unity of invention is lacking. It may be possible to rejoin
additional species of morphogen if generic subject matter is allowable.

The requirement is still deemed proper and is therefore made FINAL.

20 Claims 1, 3, 4, 21, 22, 25, 26, 28-34, 39-52 are withdrawn from further consideration
pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention and/or species, there

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being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 12.

Inventorship

5 In view of the papers filed 09/05/2000 (Paper No. 5), it has been found that this nonprovisional application, as filed, through error and without deceptive intent, improperly set forth the inventorship, and accordingly, this application has been corrected in compliance with 37 CFR 1.48(a). The inventorship of this application has been changed by adding Slobodon Vukicevic as an inventor.

10 The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt, and correction of the file jacket and PTO PALM data to reflect the inventorship as corrected.

Formal Matters

15 Citations by the examiner are in an alphanumeric format, such as "(a1)", wherein the "1" refers to the Paper No. to which the PTO-892 Notice of References Cited is attached and the "a" refers to the reference cited on the PTO-892 Notice of References Cited.

Information Disclosure Statement

20 Copies of the references cited in the information disclosure statement filed November 15, 2002 (Paper No. 13) either were not provided or they have been misplaced. Applicants are requested to submit or re-submit copies of the references for consideration by the examiner.

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Specification

This application does not contain an abstract of the disclosure as required by 37

CFR 1.72(b). An abstract on a separate sheet is required.

5

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37

CFR 1.67(a) identifying this application by application number and filing date is required. See

MPEP §§ 602.01 and 602.02.

10

The oath or declaration is defective because:

The specification to which the oath or declaration is directed has not been adequately identified. See MPEP § 601.01(a). The specification to which the oath or declaration is directed has been identified as 08/445,328. The correct identification is 09/445,328.

15

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

20

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

25

Claims 2, 5-14, 27, 35-38 are rejected under 35 U.S.C. 102(b) as being anticipated by Kuberasampath (AH, cited by Applicants). Kuberasampath discloses kidney malfunction causes a calcium and phosphate imbalance in the blood (page 3, lines 9-11) and preventing or inhibiting bone deterioration in patients undergoing dialysis (page 5, lines 23-26). Kuberasampath provides a therapeutic treatment method and composition for preventing loss of bone mass

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and/or for increasing bone mass in a mammal which includes administering to the individual a therapeutically effective morphogen in an amount and for a time sufficient to inhibit the loss of bone mass, and/or to increase bone mass in the individual (page 7, lines 8-14). The treatment methods and compositions may be used to treat any disease which causes or results in bone fractures or other defects in skeletal microstructure, including loss of bone mass, and which compromise the weight-bearing capacity of bone. Such diseases include chronic renal failure and other kidney diseases, particularly those requiring dialysis. See page 8, lines 23-31. The methods and compositions for protecting an individual at risk for the loss or deterioration of skeletal bone mass by prophylactic administration of a morphogen. Individuals at risk include individuals undergoing dialysis, particularly prolonged or chronic dialysis. See page 9, lines 1-8. The morphogen is administered systemically to the individual, e.g., orally or parenterally (page 9, lines 10-13). Among the useful morphogens are proteins originally identified as osteogenic proteins, such as the OP-1, OP-2 and CBMP2 proteins (page 11, lines 6-8). "OP-1" refers to the mature protein comprising the conserved seven cysteine skeleton (page 12, lines 3-24; page 30). A protein is morphogenic if it is capable of inducing the developmental cascade of cellular and molecular events that culminate in the formation of new, organ-specific tissue and comprises at least the conserved C-terminal six cysteine skeleton (page 39, lines 10-14). The morphogens may be provided to an individual by any suitable means, preferably directly, parenterally or orally. Where the morphogen is to be provided directly (e.g., locally, as by injection, to a bone tissue site), or parenterally, such as by intravenous, subcutaneous, intramuscular, intraorbital, ophthalmic, intraventricular, intracranial, intracapsular, intraspinal, intracisternal, intraperitoneal, buccal, rectal, vaginal, intranasal or by aerosol administration, the morphogen preferably

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comprises part of an aqueous solution (paragraph bridging pages 48-49). The compounds may be provided in an aqueous physiological buffer solution containing about 0.1 to 10% w/v compound for parenteral administration. Typical dose ranges are from about 10 ng/kg to about 1 g/kg of body weight per day; a preferred dose range is from about 0.1 µg/kg to 100 mg/kg of body weight per day. Optimally, the morphogen dosage given in all cases is between 2-20 µg of protein per kilogram weight of the patient per day. Currently preferred dose ranges for local injection of soluble morphogen to bone tissue are 0.1-50 µg morphogen/injection. See page 54, lines 24-32. Ovariectomized rats received daily injections of approximately 2 µg of OP-1 by tail vein for 22 days (page 69, lines 13-15). The examiner deems daily injections for 22 days to be administration daily for a period of at least about one week and administration at least once a week for a period of at least about one month. The need for dialysis treatments of the rats was delayed, in the absence of evidence to the contrary.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 2, 15-20, 24, 35-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kuberasampath (AH) as applied to claim 2 above and further in view of Anderson (u14).

Kuberasampath discloses kidney malfunction causes a calcium and phosphate imbalance in the blood (page 3, lines 9-11) and preventing or inhibiting bone deterioration in patients

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undergoing dialysis (page 5, lines 23-26). Kuberasampath provides a therapeutic treatment method and composition for preventing loss of bone mass and/or for increasing bone mass in a mammal which includes administering to the individual a therapeutically effective morphogen in an amount and for a time sufficient to inhibit the loss of bone mass, and/or to increase bone mass in the individual (page 7, lines 8-14). The treatment methods and compositions may be used to treat any disease which causes or results in bone fractures or other defects in skeletal microstructure, including loss of bone mass, and which compromise the weight-bearing capacity of bone. Such diseases include chronic renal failure and other kidney diseases, particularly those requiring dialysis. See page 8, lines 23-31. The methods and compositions for protecting an individual at risk for the loss or deterioration of skeletal bone mass by prophylactic administration of a morphogen. Individuals at risk include individuals undergoing dialysis, particularly prolonged or chronic dialysis. See page 9, lines 1-8. The morphogen is administered systemically to the individual, e.g., orally or parenterally (page 9, lines 10-13). Among the useful morphogens are proteins originally identified as osteogenic proteins, such as the OP-1, OP-2 and CBMP2 proteins (page 11, lines 6-8). "OP-1" refers to the mature protein comprising the conserved seven cysteine skeleton (page 12, lines 3-24; page 30). A protein is morphogenic if it is capable of inducing the developmental cascade of cellular and molecular events that culminate in the formation of new, organ-specific tissue and comprises at least the conserved C-terminal six cysteine skeleton (page 39, lines 10-14). The morphogens may be provided to an individual by any suitable means, preferably directly, parenterally or orally. Where the morphogen is to be provided directly (e.g., locally, as by injection, to a bone tissue site), or parenterally, such as by intravenous, subcutaneous, intramuscular, intraorbital,

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ophthalmic, intraventricular, intracranial, intracapsular, intraspinal, intracisternal, intraperitoneal, buccal, rectal, vaginal, intranasal or by aerosol administration, the morphogen preferably comprises part of an aqueous solution (paragraph bridging pages 48-49). The compounds may be provided in an aqueous physiological buffer solution containing about 0.1 to 10% w/v compound for parenteral administration. Typical dose ranges are from about 10 ng/kg to about 1 g/kg of body weight per day; a preferred dose range is from about 0.1 µg/kg to 100 mg/kg of body weight per day. Optimally, the morphogen dosage given in all cases is between 2-20 µg of protein per kilogram weight of the patient per day. Currently preferred dose ranges for local injection of soluble morphogen to bone tissue are 0.1-50 µg morphogen/injection. See page 54, lines 24-32. Ovariectomized rats received daily injections of approximately 2 µg of OP-1 by tail vein for 22 days (page 69, lines 13-15). The examiner deems daily injections for 22 days to be administration daily for a period of at least about one week and administration at least once a week for a period of at least about one month. The need for dialysis treatments of the rats was delayed, in the absence of evidence to the contrary. Kuberasampath is silent with respect to decreased cardiac output and serial determination of BUN or serum creatinine.

Anderson teaches that impaired cardiac output is a major cause of acute deterioration in renal function (page 1293, Table 275-1). In acute renal failure the daily increments in BUN and serum creatinine average from 10 to 20 and 0.5 to 1.0 mg per 100 ml, respectively, to 40 to 100 and 2 to 5 mg per 100 ml, respectively (page 1296, left column, full paragraph 2). There has been an increasing tendency to use dialysis therapy early in acute renal failure (page 1298, left column, last full paragraph). Anderson does not teach treatment to delay the need for, or reduce the frequency of dialysis by administering a morphogen.

Insofar as impaired cardiac output is a major cause of acute deterioration in renal function and there has been an increasing tendency to use dialysis therapy early in acute renal failure, and insofar as kidney malfunction causes a calcium and phosphate imbalance in the blood, particularly those requiring dialysis, and cause or result in bone fractures or other defects in skeletal microstructure, including loss of bone mass, and which compromise the weight-bearing capacity of bone, and to the extent that these defects in skeletal microstructure, including loss of bone mass, which compromises the weight-bearing capacity of bone, can be treated by the administration of OP-1, then it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to administer OP-1 to a mammal afflicted with decreased cardiac output, with a reasonable expectation of success. One of ordinary skill in the art would be motivated to make this modification in order to prevent loss of bone mass and/or increase bone mass in the mammal with kidney disease or renal malfunction.

It would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to administer OP-1 to mammal wherein the daily increments in BUN and serum creatinine average from 10 to 20 and 0.5 to 1.0 mg per 100 ml, respectively, to 40 to 100 and 2 to 5 mg per 100 ml, respectively. One of ordinary skill in the art would be motivated to make this modification in order to prevent loss of bone mass and/or increase bone mass in the mammal with kidney disease or renal malfunction.

Kuberasampath (AH) as applied to claim 2 above and further in view of Anderson (u14) are silent with respect to the mammal having one or two kidneys. However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to administer OP-1 to mammal with kidney disease or renal malfunction wherein the mammal has one or two

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kidneys, with a reasonable expectation of success. One of ordinary skill in the art would be motivated to make this modification in order to prevent loss of bone mass and/or increase bone mass in the mammal with kidney disease or renal malfunction.

Where the general conditions of a claim are disclosed in the prior art, it is not inventive to
5 discover the optimum or workable ranges by routine experimentation.

The invention is prima facie obvious over the prior art.

Claims 2, 23, 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over
Kuberasampath (AH, cited by Applicants) as applied to claim 2 above, and further in view of
10 Spragg (a14), Saavedra (b14), and Kuberasampath (AG, cited by Applicants).

The teachings of Kuberasampath (AH) are discussed above. Kuberasampath (AH) is silent with respect to a kidney transplant recipient or a mammal having only one kidney.

Spragg (a14) teaches that recipients of cadaver allografts are frequently oliguric and dialysis-dependent due to acute tubular necrosis (paragraph bridging columns 1-2).

15 Saavedra (b14) teaches that episodes of ischemia reperfusion are associated with kidney transplants and that protecting against adverse consequences of shock, such as kidney dysfunction can be accomplished by preventing neutrophil adherence (paragraph bridging columns 11-12).

Kuberasampath teaches the administration of a morphogen, OP1, to a transplant recipient
20 (page 4, line 26; page 7, lines 29-33; page 12, line 30, through page 13, line 21). Kuberasampath teaches that damage to cells resulting from the effects of an inflammatory response by immune cell mediated tissue destruction has been implicated as the cause of reduced tissue function or

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loss of tissue function in the kidney; glomerulonephritis is believed to result in large part from unwanted acute inflammatory reactions and fibrosis (page 1, lines 21-33). The immune cell mediated tissue destruction often follows an initial tissue injury or insult; the secondary damage often is the source of significant tissue damage (page 2, lines 7-11). When the interruption of blood flow limits the oxygen supply to the proximal tubular cells of the kidney the cells may become irreversibly injured and the ensuing inflammatory responses to this initial injury provide additional insult to the affected tissue (page 3, full paragraph 1). The morphogen may be provided directly to the tissue (paragraph bridging pages 11-12). OP1 (page 14, line 30, through page 15, line 17) inhibits the adherence of LTB₄ activated PMNs to endothelium (Example 5, pages 74-75), inhibits cellular and humoral inflammatory reactions (Example 7, pages 78-80), and inhibits epithelial cell proliferation (Example 10, page 86-87).

Spragg, Saavedra, and Kuberasampath (AG) are silent with respect to the administration of a morphogen to a kidney transplant recipient or a mammal with only one kidney.

However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to administer OP-1 to a mammal undergoing dialysis, as taught by Kuberasampath (AH), and to modify that teaching by administering OP-1 to a kidney transplant recipient, with a reasonable expectation of success. One of ordinary skill in the art would be motivated to make this modification because recipients of cadaver allografts are frequently oliguric and dialysis-dependent due to acute tubular necrosis and the administration of OP-1 would prevent loss of bone mass and/or increase bone mass in the mammal with kidney malfunction or diseases or undergoing dialysis. One of ordinary skill in the art would be further motivated to make this modification because episodes of ischemia reperfusion are associated

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with kidney transplants, protecting against adverse consequences of shock, such as kidney dysfunction can be accomplished by preventing neutrophil adherence, and OP-1 inhibits neutrophil adherence, and in order to prevent loss of bone mass and/or increase bone mass in the mammal undergoing dialysis or with kidney disease or renal malfunction.

5 It would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to administer OP-1 to a kidney transplant recipient wherein either one or two kidneys had been transplanted, with a reasonable expectation of success. One of ordinary skill in the art would be motivated to make this modification because episodes of ischemia reperfusion are associated with kidney transplants, protecting against adverse consequences of shock, such as kidney dysfunction can be accomplished by preventing neutrophil adherence, and OP-1 inhibits neutrophil adherence, and in order to prevent loss of bone mass and/or increase bone mass in the mammal undergoing dialysis or with kidney disease or renal malfunction.

The invention is prima facie obvious over the prior art.

15 *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

20 The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2, 5, 7-20, 23, 24, 27, 35-38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treatment comprising

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administering OP-1 to a mammal, does not reasonably provide enablement for a method of treatment comprising administering the other OP/BMP renal therapeutic agents recited in the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The scope of the claims include numerous structural variants of OP-1. There is a lack of predictability in the art. Predicting structure, hence function, from primary amino acid sequence data is extremely complex and there doesn't exist an efficient algorithm for predicting the structure of a given protein from its amino acid sequence alone. See Bowie (v14) page 1306, column 1, full paragraph 1, or Ngo (w14) page 433, full paragraph 1, and page 492, full paragraph 2. Vukicevic (x14) teaches that OP-1 promotes cell condensations and tubulogenesis in metanephric mesenchyme but BMP-2, a closely related member of the TGF-superfamily, and TGF-1 had no effect (page 9023, paragraph bridging columns 1-2). Vukicevic establishes that closely related members of the TGF- β superfamily have unpredictable effects. The only working examples in the specification are with OP-1. There are no working examples of other OP/BMP renal therapeutic agents. Other than claim 13, the claims do not recite a clear functional limitation to the OP/BMP renal therapeutic agents. The specification provides no guidance as to which of the myriad of structural embodiments are more likely than not to function in the manner disclosed. The skilled artisan is left to extensive experimentation wherein OP/BMP renal therapeutic agents are randomly made and through trial and error experimentation is left to determine how to achieve the desired results. In view of the breadth of the claims, the limited amount of direction and working examples provided by the inventor, the unpredictability in the art and the quantity of experimentation needed to make or use the invention based on the

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content of the disclosure, it would require undue experimentation for the skilled artisan to make and/or use the full scope of the claimed invention.

The following claims are rejected under 35 U.S.C. 112, second paragraph, as being
5 indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2, 15-20, 23, 24, 27, 35-38 are indefinite because they recite the term "OP/BMP
renal therapeutic agent". Because the instant specification does not identify that material
element or combination of elements which is unique to, and, therefore, definitive of "OP/BMP
10 renal therapeutic agent" an artisan cannot determine what additional or material functional limitations are placed upon a claim by the presence of this element. The metes and bounds are not clearly set forth.

Claims 5, 6, 13 are indefinite over the recitation of "a C-terminal cysteine domain"
because it is unclear if the C-terminal seven cysteine domain or some portion of the C-terminal
15 seven cysteine domain is intended. The metes and bounds are not clearly set forth.

Claims 7-13 are indefinite over the recitation of "an amino acid sequence of a seven
cysteine domain" because it is unclear of the amino acid sequence of a seven cysteine domain or
some portion of the amino acid sequence of a seven cysteine domain is intended. The metes and
bounds are not clearly set forth.

20

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or

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improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 2, 5-20, 23, 24, 27, 35-38 rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4, 6, 10, 12, 15-17, 24, 28, 32, 52-55 of copending application no. 08851628. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the present application are generic to and encompass the claims of the co-pending application.

Claims 2, 5-20, 23, 24, 27, 35-38 rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims of copending application no. 08/643,321, which will issue as patent no. 6498142 on 12/24/2002. The claims of 08643321 are unavailable to the examiner. This rejection is being made in the event that the claims of the copending application are directed to or encompass treatment with a morphogen to delay the need for, or reduce the frequency of dialysis treatments.

Conclusion

No claims are allowable.

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ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (703) 305-4050. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M.

IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, GARY KUNZ, CAN BE REACHED ON (703) 308-4623.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE FOLLOWING TC 1600 BEFORE AND AFTER FINAL RIGHTFAX NUMBERS:

BEFORE FINAL (703) 872-9306

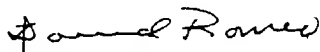
AFTER FINAL (703) 872-9307

IN ADDITION TO THE OFFICIAL RIGHTFAX NUMBERS ABOVE, THE TC 1600 FAX CENTER HAS THE FOLLOWING OFFICIAL FAX NUMBERS: (703) 305-3592, (703) 308-4242 AND (703) 305-3014.

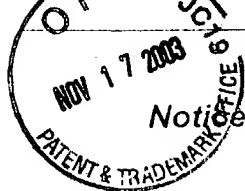
CUSTOMERS ARE ALSO ADVISED TO USE CERTIFICATE OF FACSIMILE PROCEDURES WHEN SUBMITTING A REPLY TO A NON-FINAL OR FINAL OFFICE ACTION BY FACSIMILE (SEE 37 CFR 1.6 AND 1.8).

FAXED DRAFT OR INFORMAL COMMUNICATIONS SHOULD BE DIRECTED TO THE EXAMINER AT (703) 308-0294.

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.


DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647

DSR
DECEMBER 15, 2002



Notice of References Cited

Application/Control No.

09/445,328

Applicant(s)/Patent Under
Reexamination
SAMPATH ET AL.

Examiner

David S Romeo

Art Unit

1647

Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
	A	US-5,045,452	09-1991	Spragg et al.	435/7.4
	B	US-5,714,511	02-1998	Saavedra et al.	514/426
	C	US-			
	D	US-			
	E	US-			
	F	US-			
	G	US-			
	H	US-			
	I	US-			
	J	US-			
	K	US-			
	L	US-			
	M	US-			

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	Classification
	N					----
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	Anderson et al. "Acute Renal Failure", Chapter 275 in Harrison's principles of internal medicine, 9th ed., editors, Kurt J. Isselbacher et al, New York : McGraw-Hill, c1980, page 1296.
	V	Bowie et al. Deciphering the message in protein sequences: tolerance to amino acid substitutions. Science, (1990 Mar 16) 247 (4948) 1306-10.
	W	Ngo et al., in The Protein Folding Problem and Tertiary Structure Prediction, Merz and Le Grand (Eds), August 1994, Springer Verlag, pages 433 and 492-495.
	X	Vukicevic et al. Induction of nephrogenic mesenchyme by osteogenic protein 1 (bone morphogenetic protein 7). Proc Natl Acad Sci U S A 1996 Aug 20;93(17):9021-6.

A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.